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NEWS 2		"Ask CAS" for self-help around the clock
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NEWS 4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 12	OCT 19	The Derwent World Patents Index suite of databases on STN will be enhanced and reloaded on October 22, 2006
NEWS 13	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 14	OCT 19	E-mail format enhanced

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=> s 22494-47-9/rn or clozic acid or clobuzarit or clozic
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L1          176 22494-47-9/RN OR CLOZIC ACID OR CLOBUZARIT OR CLOZIC

=> s 76496-49-6/rn or 76431-92-0/rn or 76431-90-8/rn or 76431-89-5/rn or
76431-88-4/rn or 76431-87-3/rn or 76431-85-1/rn or 76431-84-0/rn
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
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                OR 76431-88-4/RN OR 76431-87-3/RN OR 76431-85-1/RN OR 76431-84-
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=> s 80565-35-1/rn or 76496-48-5/rn or 76431-97-5/rn or 76431-96-4/rn or
76431-95-3/rn or 76431-93-1/rn or 76431-92-0/rn or 76431-91-9/rn or 76431-90-8/rn
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
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                OR 76431-95-3/RN OR 76431-93-1/RN OR 76431-92-0/RN OR 76431-91-
                9/RN OR 76431-90-8/RN

=> s l1 or l2 or l3
L4          180 L1 OR L2 OR L3

=> s l4 and (diabete or glucose or kidney or nephro? )
L5            8 L4 AND (DIABETE OR GLUCOSE OR KIDNEY OR NEPHRO? )

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6            8 DUP REM L5 (0 DUPLICATES REMOVED)

=> d ibib abs hitstr 1-8

L6   ANSWER 1 OF 8  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:   2005530655  EMBASE
TITLE:              Drugs to treat inflammation: A historical introduction.
AUTHOR:             Whitehouse M.W.
CORPORATE SOURCE:   M.W. Whitehouse, PO Box 68, Stones Corner, QLD 4120,
                    Australia. whitehousemd@spin.net.au
SOURCE:             Current Medicinal Chemistry, (2005) Vol. 12, No. 25, pp.
                    2931-2942. .
                    Refs: 22
                    ISSN: 0929-8673  CODEN: CMCHE7
COUNTRY:            Netherlands
DOCUMENT TYPE:      Journal; General Review
FILE SEGMENT:       005     General Pathology and Pathological Anatomy
                    031     Arthritis and Rheumatism
                    037     Drug Literature Index
```

038 Adverse Reactions Titles
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Dec 2005
Last Updated on STN: 29 Dec 2005

AB Drugs to treat inflammation are discussed under the following headings: (1) random discoveries covering copper, salicylates, heterocyclic diones, ACTH, adrenal steroids and disease-modifying agents (DMARDs); these include Au(I)-thiolates, chloroquine, and hydroxychloroquine, minocycline, cyclosporin, salazopyrine, D-penicillamine and methotrexate; (2) programmed NSAID developments covering salicylates and fenamates, arylalkanoates, diones, non-acidic NSAIDs, **clozic**, lobenzarit and coxibs; (3) synthetic glucocorticosteroids; and (4) 'Biologicals' for neutralising pro-inflammatory cytokines. Clinical problems are highlighted, particularly unacceptable side-effects affecting the GI tract, skin, liver, etc. that caused many drugs to be withdrawn. Drug combinations may overcome some of these problems. The bibliography has selected reviews and monographs covering 50 years of publications.

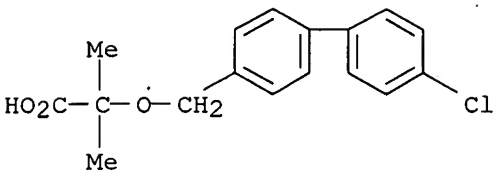
L6 ANSWER 2 OF 8 CAPLUS
ACCESSION NUMBER: 2005:699596 CAPLUS
DOCUMENT NUMBER: 144:344703
TITLE: Human toxicological effect and damage factors of carcinogenic and noncarcinogenic chemicals for life cycle impact assessment
AUTHOR(S): Huijbregts, Mark A. J.; Rombouts, Linda J. A.; Ragas, Ad M. J.; van de Meent, Dik
CORPORATE SOURCE: Department of Environmental Science, Institute for Wetland and Water Research, Faculty of Science, Radbound University Nijmegen, Nijmegen, 6500GL, Neth.
SOURCE: Integrated Environmental Assessment and Management (2005), 1(3), 181-244
CODEN: IEAMCK; ISSN: 1551-3777
PUBLISHER: Society of Environmental Toxicology and Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chemical fate, effect, and damage should be accounted for in the anal. of human health impacts by toxic chems. in life cycle assessment (LCA). The goal of this article is to present a new method to derive human damage and effect factors of toxic pollutants, starting from a lognormal dose-response function. Human damage factors are expressed as disability-adjusted life-years (DALYs). Human effect factors contain a disease-specific and a substance-specific component. The disease-specific component depends on the probability of disease occurrence and the distribution of sensitivities in the human population. The substance-specific component, equal to the inverse of the ED50, represents the toxic potency of a substance. The new method has been applied to calculate combined human damage and effect factors for 1192 substances. The total range of 7-9 orders of magnitude between the substances is dominated by the range in toxic potencies. For the combined factors, the typical uncertainty, represented by the square root of the ratio of the 97.5th and 2.5th percentiles, is a factor of 25 for carcinogenic effects and a factor of 125 for noncarcinogenic effects. The interspecies conversion factor, the (non)cancer effect conversion factor, and the average noncancer damage factor dominate the overall uncertainty.

IT **22494-47-9, Clobuzarit**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (human toxicol. effect and damage factors of carcinogenic and noncarcinogenic chems. for life cycle impact assessment)

RN 22494-47-9 CAPLUS
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)methoxy]-2-methyl- (9CI)

(CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 8 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 95155909 EMBASE
DOCUMENT NUMBER: 1995155909
TITLE: Adverse drug reactions and their measurement in the rheumatic diseases.
AUTHOR: Day R.O.; Quinn D.I.; Conaghan P.G.; Tett S.E.
CORPORATE SOURCE: Dept.of Clin.Pharmacology/Toxicology, St. Vincent's Hospital, Victoria St.,Darlinghurst, NSW 2010, Australia
SOURCE: Journal of Rheumatology, (1995) Vol. 22, No. 5, pp. 983-988. .
ISSN: 0315-162X CODEN: JRHUA
COUNTRY: Canada
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
031 Arthritis and Rheumatism
052 Toxicology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jun 1995
Last Updated on STN: 19 Jun 1995

AB Drugs administered as therapy for rheumatological disorders are a relatively common cause of adverse events. Important data regarding the effects of drugs on patients with rheumatological conditions is being lost or rendered inaccessible because of deficiencies in classification, measurement, and collection methods for adverse drug reactions. A significant number of adverse reactions to drugs will not be known before marketing, and hence vigilance on the part of clinicians and patients in observing and documenting these reactions is paramount in building our knowledge and modifying our practice accordingly. A variety of systems and methods for detecting adverse drug reactions are described, critically evaluated, and compared for cost, potential bias, ethical concerns, and subject recruitment required for necessary statistical power. Systems need to be developed to give access to the wealth of clinical experiential data available in the individual practices of a broad spectrum of clinicians. To facilitate this, representative organizations need to make adverse drug reactions a high priority as well as contributing expertise and finance to database formulation and accessibility.

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ACCESSION NUMBER: 90127793 EMBASE
DOCUMENT NUMBER: 1990127793
TITLE: Biologic properties of romazarit (Ro 31-3948), a potential disease-modifying antirheumatic drug.
AUTHOR: Bloxham D.P.; Bradshaw D.; Cashin C.H.; Dodge B.B.; Lewis

E.J.; Westmacott D.; Self C.R.
CORPORATE SOURCE: Biology Department, Roche Products Ltd.,Herts AL7 3AY, United Kingdom
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1990) Vol. 252, No. 3, pp. 1331-1340. .
ISSN: 0022-3565 CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
014 Radiology
029 Clinical Biochemistry
031 Arthritis and Rheumatism
052 Toxicology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991

AB The biologic effects of a new potential disease-modifying antirheumatic drug, romazarit (Ro 31-3948, 2-[[2-(4-chlorophenyl)-4-methyl-5-oxazolyl]-2-methylpropionic acid), have been investigated. In a 5-day adjuvant arthritis model, romazarit inhibited the development of hindpaw inflammation with a minimum effective dose of 30 mg kg-1. Plasma levels of the acute phase reactants seromucoid and haptoglobulin were also significantly reduced. Romazarit was equally effective in adrenalectomized animals, indicating that the compound is not acting via stimulation of the pituitary/adrenal axis. When the developing adjuvant arthritis was extended to 15 days romazarit showed dose-related improvements of all the symptoms of arthritis with a minimum effective dose of 25 mg kg-1. Romazarit caused a dose-dependent (range 20-250 mg kg-1) reduction in both the inflammatory and bony changes occurring during collagen arthritis in the rat, without any significant effect on anticollagen antibody titers except at the highest dose. Collagenase and prostaglandin E2 production in cultures of talus bones taken from rats with collagen arthritis were reduced by romazarit. In vitro romazarit was an extremely weak inhibitor of prostaglandin synthetase activity in both sheep seminal vesicle (IC50 6500 μM) and rat renal medulla (IC50 > 300 μM) cell-free preparations. Romazarit showed little or no activity in models of acute inflammation such as rabbit skin edema, carrageenan pleurisy or UV-induced erythema. In both acute and chronic tests romazarit displayed no ulcerogenic potential. In comparison with the structurally similar compound **clobuzarit**, hepatic changes such as increases in catalase and peroxisome proliferation-associated 80,000 mol.weight protein were markedly less with romazarit. Clinical studies with romazarit are currently in progress.

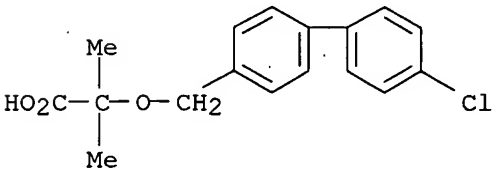
L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:567129 CAPLUS
DOCUMENT NUMBER: 111:167129
TITLE: Differential induction of peroxisomal and microsomal fatty-acid-oxidizing enzymes by peroxisome proliferators in rat liver and **kidney**. Characterization of a renal cytochrome P-450 and implications for peroxisome proliferation
AUTHOR(S): Sharma, Rajesh K.; Lake, Brian G.; Makowski, Richard; Bradshaw, Tony; Earnshaw, Dave; Dale, Jeremy W.; Gibson, G. Gordon
CORPORATE SOURCE: Dep. Biochem., Univ. Surrey, Guildford, GU2 5XH, UK
SOURCE: European Journal of Biochemistry (1989), 184(1), 69-78
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The induction of renal fatty-acid oxidizing enzymes was investigated followed short-term exposure to a group of structurally diverse peroxisome proliferators and compared to the more extensively documented hepatic responses in the rat. There was a marked compound dependence on induction of both cytochrome P 450-IVA1-dependent ω-hydroxylation of lauric acid and enzymes of the peroxisomal fatty acid β-oxidation pathway (measured as cyanide-insensitive palmitoyl-CoA oxidation and enoyl-CoA hydratase). Cytochrome P 450 IVA1 (or a very closely related isoenzyme in the same gene family) was a major constitutive hemoprotein in rat **kidney** microsomes and actively supported the ω-hydroxylation of lauric acid. This activity was induced 2-3-fold by peroxisome proliferators such as clofibrate, di-(2-ethylhexyl)phthalate, bezafibrate, and nafenopin. By using a cDNA probe to the cytochrome P 450 IVA1 gene in Northern blot anal. it was shown that increased renal and hepatic ω-hydroxylation of lauric acid, after treatment with peroxisome proliferators is a consequence of a substantial increase in the mRNA coding for this hemoprotein. In addition, programming of an in vitro rabbit reticulocyte translation system with both renal and hepatic RNA resulted in the synthesis of similar (if not identical) cytochrome-P 450-IVA1-related polypeptides. Furthermore, Western blot evidence was provided that both rat liver and **kidney** microsomes contain 2 closely related cytochrome P 450 IVA1 polypeptides, the major one characterized by a monomeric mol. mass of 51.5 kDa (identical to authentic, purified hepatic cytochrome P 450 IVA1) and a minor one of 52 kDa. The **kidney**-supported fatty acid ω-hydroxylase activity was refractory to inhibition by a polyclonal antibody to liver cytochrome P 450 IVA1, which may be related to the existence of 2 closely related (but immunochem. distinct) fatty acid hydroxylases in this tissue. Certain of the compds. tested (including clofibrate, bezafibrate, and nafenopin) induced renal fatty acid β-oxidation, mirroring the increased ω-hydroxylase activity in the endoplasmic reticulum. The **kidney** was more refractory to induction of the endoplasmic reticulum and peroxisomal fatty-acid-oxidizing enzymes than was the liver. This suggests a possible linkage of the renal fatty acid oxidative enzymes in these 2 organelles, a situation that also occurs in the liver. In addition, a possible conceptual framework that may rationalize the decreased susceptibility of the **kidney** to the toxicity of peroxisome proliferators is provided.

IT **22494-47-9, Clobuzarit**
RL: BIOL (Biological study)
(fatty acid-oxidizing enzymes of microsome or peroxisome of, hypolipemics induction of)

RN 22494-47-9 CAPLUS

CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)methoxy]-2-methyl- (9CI) (CA INDEX NAME)



L6 ANSWER 6 OF 8 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 88101188 EMBASE
DOCUMENT NUMBER: 1988101188
TITLE: The effects of peroxisome proliferators on microsomal, peroxisomal, and mitochondrial enzyme activities in the liver and **kidney**.

AUTHOR: Hawkins J.M.; Jones W.E.; Bonner F.W.; Gibson G.G.
CORPORATE SOURCE: Biochemistry Department, Division of Pharmacology and Toxicology, University of Surrey, Guidford GU2 5XH, United Kingdom
SOURCE: Drug Metabolism Reviews, (1987) Vol. 18, No. 4, pp. 441-515. .
ISSN: 0360-2532 CODEN: DMTRAR
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
035 Occupational Health and Industrial Medicine
052 Toxicology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Dec 1991
Last Updated on STN: 11 Dec 1991

AB In recent years a growing concern has developed about the long-term exposure of man to hypolipidemic drugs and industrial plasticizers, and its possible effect on human health. This concern is based largely on the ever-increasing evidence that compounds capable of inducing peroxisome proliferation in rodent liver also induce hepatocellular carcinomas in rats and mice. Fro the outset it must be emphasized that although the rodent responses to peroxisome proliferation are amply documented, there is an intense controversy regarding the relevance of rodent data to other species, particularly nonhuman primates and man. In this review, the subcellular responses of rodents to treatment with hypolipidemic agents are described at some length. The implications of these biochemical and ultrastructural changes in rodents are discussed with reference to the exhibited hypolipidemic effect and to the relevance of extrapolating animal toxicity data to assess potential human health hazard.

L6 ANSWER 7 OF 8 EMBASE
ACCESSION NUMBER: 82109839 EMBASE
DOCUMENT NUMBER: 1982109839
TITLE: Slow-acting antirheumatic drugs.
AUTHOR: Mowat A.G.
CORPORATE SOURCE: Nuffield Orthop. Cent., Univ. Oxford, Oxford, United Kingdom
SOURCE: South African Medical Journal, (1982) Vol. 61, No. 10, pp. 346-348. .
CODEN: SAMJAF
COUNTRY: South Africa
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
031 Arthritis and Rheumatism
030 Pharmacology
006 Internal Medicine
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

AB Rheumatoid arthritis can be controlled by the use of an increasing range of slow-acting drugs and treatments whose mode of action, currently unexplained or lacking a rational basis, may eventually provide a better understanding of the disease.

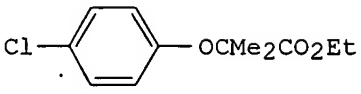
L6 ANSWER 8 OF 8 CAPLUS
ACCESSION NUMBER: 1981:114449 CAPLUS
DOCUMENT NUMBER: 94:114449

TITLE: Induction by oxyisobutyrates of hepatic and **kidney** microsomal cytochrome P-450 with specificity towards hydroxylation of fatty acids

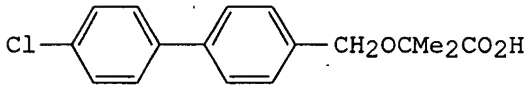
AUTHOR(S): Parker, G. L.; Orton, T. C.
CORPORATE SOURCE: Saf. Med. Dep., ICI, Macclesfield/Cheshire, UK

SOURCE: Developments in Biochemistry (1980), 13(Biochem., Biophys. Regul. Cytochrome P-450), 373-7
CODEN: DEBIDR; ISSN: 0165-1714
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



I



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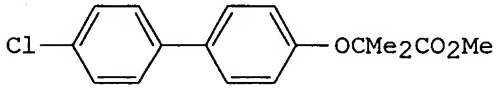


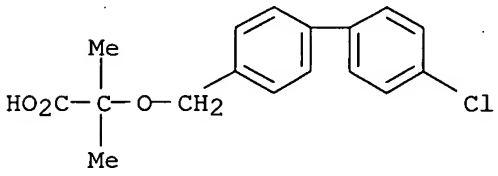
III

AB Rats fed diets containing 0.4% clofibrate (I) [637-07-0], 0.05% **Clozic** (II) [**22494-47-9**], or 0.005% methylclofenapate (III) [21340-68-1] showed a marked increase in liver microsomal cytochrome P 450 [9035-51-2]; II also produced a consistent increase in **kidney** cortex microsomal cytochrome P 450. The oxyisobutyrates markedly induced the cytochrome P 450 in liver microsomes which specifically catalyzed the ω-hydroxylation of lauric acid [143-07-7].

IT **22494-47-9**
RL: BIOL (Biological study)
(cytochrome P 450 induction by, in **kidney** and liver, fatty acid hydroxylation in relation to)

RN 22494-47-9 CAPLUS

CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)methoxy]-2-methyl- (9CI) (CA INDEX NAME)



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L2             5 S 76496-49-6/RN OR 76431-92-0/RN OR 76431-90-8/RN OR 76431-89-5
L3             5 S 80565-35-1/RN OR 76496-48-5/RN OR 76431-97-5/RN OR 76431-96-4
L4           180 S L1 OR L2 OR L3
L5             8 S L4 AND (DIABETE OR GLUCOSE OR KIDNEY OR NEPHRO? )
L6             8 DUP REM L5 (0 DUPLICATES REMOVED)

     FILE 'CAPLUS' ENTERED AT 15:46:24 ON 20 OCT 2006
L7             1 S WO 9962507/PN
                 SEL L7
L8             0 S C23H21CL03 OR C17H17CL03
L9       1406767 S E1-E11
L10        50174 S L9 AND (DIABETE? OR NEPHRO? OR GLUCOSE)
L11            0 S L10 AND (80565-35-1/RN OR 22494-47-9/RN)

=>
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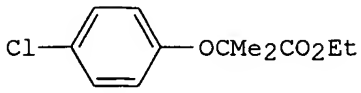
L31 ANSWER 13 OF 96 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:461665 CAPLUS
DOCUMENT NUMBER: 93:61665
TITLE: Some platelet function tests normalized by ICI 55, 897 and by clofibrate
AUTHOR(S): O'Brien, J. R.
CORPORATE SOURCE: Cent. Lab., St. Mary's Hosp., Portsmouth, UK
SOURCE: Proceedings of the Serono Symposia (1979), Volume Date 1977, 15(Haemostasis Thromb.), 403-6
CODEN: PSSYDG; ISSN: 0308-5503
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

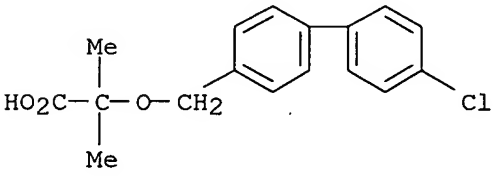


I

AB Clofibrate (I) [637-07-0] administration to patients with either recurrent myocardial **infarct**, deep vein **thrombosis**, or transient ischemic attacks normalized heparin **thrombin** clotting time (HTCT) but further decreased anti-**thrombin** activity. The changes in the platelet function test were not correlated with the I-induced changes in plasma cholesterol or triglycerides. ICI 55897 [**22494-47-9**], an analog of I, when administered to these patients also normalized HTCT, decreased fibrinogen, but hardly affected antithrombic activity. The unchanged decrease in antithrombic activity following I administration must be regarded as an undesirable effect of the drug and thus ICI 55897 may be a more useful drug.

IT **22494-47-9**
RL: BIOL (Biological study)
(blood platelet function response to, antithrombin activity in relation to)

RN 22494-47-9 CAPLUS
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)methoxy]-2-methyl- (9CI) (CA INDEX NAME)



ATENT ASSIGNEE(S): Imperial Chemical Industries Limited, London, England (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4310544		19820112	<--
APPLICATION INFO.:	US 1980-203225		19801031 (6)	

RELATED APPLN. INFO.: Continuation of Ser. No. US 1979-66469, filed on 13 Aug 1979, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1978-36173	19780908

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Friedman, Stanley J.
LEGAL REPRESENTATIVE: Cushman, Darby & Cushman
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1,11
LINE COUNT: 544
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns novel 2-[4-(4-chlorophenyl)benzyloxy]acetic acids of the formula: ##STR1## in which R.sup.1 is hydrogen or (1-4C)alkyl, R.sup.2 is phenyl optionally bearing a halogeno substituent, and R.sup.3 is hydrogen or (1-4C)alkyl, and when R.sup.3 is hydrogen pharmaceutically acceptable base-addition salts thereof; and processes for their manufacture.

The compounds possess useful anti-arthritic properties coupled with desirable pharmacokinetic properties and the minimum of adverse properties, and the invention also concerns pharmaceutical compositions of such compounds for use in the treatment of arthritic joint diseases. A typical compound of the invention is 2-[4-(4-chlorophenyl)benzyloxy]-2-phenyl propionic acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Inflammation inhibitors
(chlorobiphenylylalkoxyalkanoic acids)

IT 79-03-8 79-30-1
(Friedel-Crafts reaction of, with chlorobiphenyl)

IT 2051-62-9
(Friedel-Crafts reaction of, with propionyl chloride)

IT 76431-63-5P
(preparation and antiinflammatory activity of)

IT 76431-76-0P
(preparation and reaction of, with bromoacetate)

IT 76431-81-7P
(preparation and reaction of, with bromoalkanoate)

IT 76431-64-6P
(preparation and reaction of, with bromopropionate)

IT 5525-72-4P 58158-34-2P 76431-79-3P
(preparation and reduction of)

IT 76431-62-4P 76431-66-8P 76431-69-1P 76431-70-4P 76431-73-7P
76431-75-9P 76431-77-1P 76600-39-0P
(preparation and saponification of)

IT 76431-65-7P 76431-67-9P 76431-68-0P 76431-71-5P 76431-72-6P
76431-74-8P 76431-78-2P 76431-80-6P 76431-82-8P
(preparation of)

IT 69231-75-0
(reaction of, with bromopropionate)

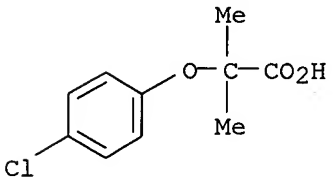
IT 105-36-2 533-68-6 535-11-5 609-12-1 615-83-8
(reaction of, with chlorobiphenylylalkanols)

L15 ANSWER 7 OF 78 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1974:22828 CAPLUS
DOCUMENT NUMBER: 80:22828
TITLE: Effect of propranolol and chlorophenoxyisobutyric acid on the dynamics of free fatty acids and blood sugar
AUTHOR(S): Haller, H.; Julius, U.; Leonhardt, W.; Hanefeld, M.
CORPORATE SOURCE: Med. Klin., Med. Akad. "Carl Gustav Carus", Dresden, Ger. Dem. Rep.
SOURCE: Deutsche Zeitschrift fuer Verdauungs- und Stoffwechselkrankheiten (1972), 32(5-6), 391-9
CODEN: DZVSAT; ISSN: 0012-1053
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The administration of 2-(4-chlorophenoxy)-2-methylpropanoic acid (Regadrin) [**882-09-7**] 4 times daily in 500 mg doses to insulin-taking **diabetics** having unbalanced metabolism produced a decrease in the blood free fatty acid level regardless of the metabolic state of the original material consumed. The **glucose** [50-99-7] assimilation coefficient was improved, but significant changes in the daily blood sugar profile did not occur and hypoglycemia was not observed Propranolol (I) [525-66-6] given 4 times daily in 25 mg doses decrased the blood free fatty acid level in the **diabetics** but did not affect carbohydrate degradation I can, nevertheless, be useful in subjects with advanced sympathicotonia and unbalanced metabolism The effect of Regadrin on blood free fatty acid level was reversible and did not continue after drug administration ceased. Precautions for use of I and Regadrin in cases of **diabetes** nellitus are discussed.

IT **882-09-7**
RL: BIOL (Biological study)
(blood sugar and fatty acid metabolism in **diabetes** in response to)

RN 882-09-7 CAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl- (9CI) (CA INDEX NAME)

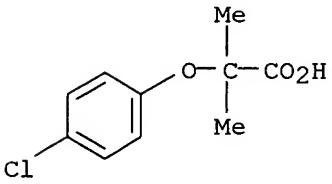


L15 ANSWER 4 OF 78 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:558280 CAPLUS
DOCUMENT NUMBER: 131:317717
TITLE: Novel Inhibitors of Advanced Glycation Endproducts
AUTHOR(S): Rahbar, Samuel; Kumar Yernini, Kiran; Scott, Stephen; Gonzales, Noe; Lalezari, Iraj
CORPORATE SOURCE: Department of Diabetes, Endocrinology & Metabolism, City of Hope National Medical Center, Duarte, CA, 91010-0269, USA
SOURCE: Biochemical and Biophysical Research Communications (1999), 262(3), 651-656
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Enhanced formation and accumulation of advanced glycation endproducts (AGE's) have been proposed to play a major role in the pathogenesis of **diabetic** complications, aging, **atherosclerosis**, and Alzheimer disease leading to progressive and irreversible intermol. protein crosslinkings. This process is accelerated in **diabetes** and has been postulated to contribute to the development of a range of **diabetic** complications including **nephropathy**, **retinopathy** and **neuropathy**. Several potential drug candidates as AGE inhibitors have been reported recently. Aminoguanidine is the first drug extensively studied both in vitro and in vivo. The authors have developed a new class of compds. as potent inhibitors of glycation and AGE formation. The novel inhibitors reported here are aryl (and heterocyclic) ureido, and aryl (and heterocyclic) carboxamido phenoxy isobutyric acids and related mols., which were found by in vitro assay methods to be potent inhibitors of multiple stage of glycation and AGE formation. (c) 1999 Academic Press.

IT **882-09-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel inhibitors of advanced glycation endproducts)

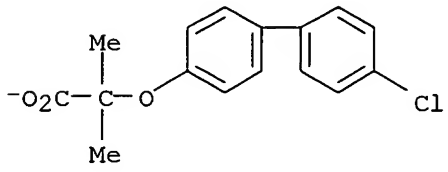
RN 882-09-7 CAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl- (9CI) (CA INDEX NAME)



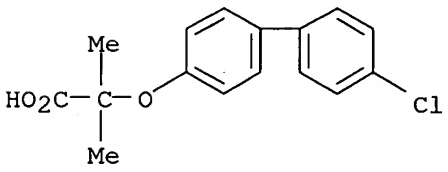
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 24578-76-5 REGISTRY
ED Entered STN: 16 Nov 1984
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methyl-, ion(1-) (9CI) (CA INDEX NAME)
MF C16 H14 Cl O3



L25 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 21345-24-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN Propionic acid, 2-[(4'-chloro-4-biphenylyl)oxy]-2-methyl-, calcium salt (8CI) (CA INDEX NAME)
MF C16 H15 Cl O3 . 1/2 Ca
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB
CRN (21340-66-9)

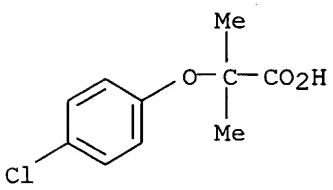


●1/2 Ca

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 21345-23-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methyl-, sodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propionic acid, 2-[(4'-chloro-4-biphenylyl)oxy]-2-methyl-, sodium salt (8CI)
OTHER NAMES:
CN Clofenapate sodium
MF C16 H15 Cl O3 . Na
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER
CRN (21340-66-9)

L15 ANSWER 6 OF 78 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:440988 CAPLUS
DOCUMENT NUMBER: 85:40988
TITLE: Effect of reduction of myocardial free fatty acid metabolism relative to that of **glucose** on the ischemic injury during experimental coronary artery occlusion in dogs
AUTHOR(S): Mjoes, Ole D.
CORPORATE SOURCE: Inst. Med. Biol., Univ. Tromsoe, Tromsoe, Norway
SOURCE: Acta Medica Scandinavica, Supplementum (1976), 587, 29-34
CODEN: AMSSAQ; ISSN: 0365-463X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Acute exptl. myocardial ischemic injury in dogs was effectively reduced by agents which reduced myocardial extraction of free fatty acids (antilipolytic agents and lipid-free albumin), thus indirectly favoring myocardial **glucose** [50-99-7] metabolism, or by agents like Na dichloroacetate [2156-56-1] which appear to enhance the utilization of **glucose** relative to that of free fatty acid.
IT **882-09-7**
RL: BIOL (Biological study)
(**heart** ischemia response to, fatty acids and **glucose** metabolism in relation to)
RN 882-09-7 CAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl- (9CI) (CA INDEX NAME)



L18 ANSWER 31 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1974:137183 CAPLUS
DOCUMENT NUMBER: 80:137183
TITLE: Phenformin clofibrate
INVENTOR(S): Hurka, Wilhelm
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2247378	A1	19740321	DE 1972-2247378	19720927 <--
AT 317235	B	19740826	AT 1972-7252	19720822 <--

PRIORITY APPLN. INFO.: AT 1972-7252 A 19720822

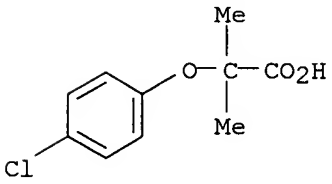
AB Phenformin clofibrate, useful for the treatment of the arteriosclerosis accompanied by **diabetes** and obesity, was prepared from clofibric acid and phenformin, obtained from its hydrochloride by common methods.

IT **52721-81-0**
RL: BIOL (Biological study)
(arteriosclerosis treatment with)

RN 52721-81-0 CAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl-, compd. with N-(2-phenylethyl)imidodicarbonimidic diamide (1:1) (9CI) (CA INDEX NAME)

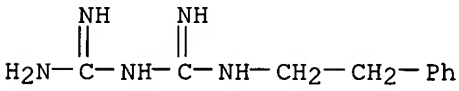
CM 1

CRN 882-09-7
CMF C10 H11 Cl O3



CM 2

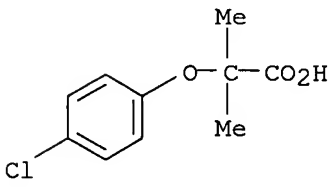
CRN 114-86-3
CMF C10 H15 N5



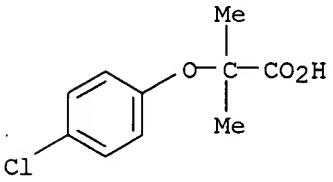
L18 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:507356 CAPLUS
DOCUMENT NUMBER: 67:107356
TITLE: Mode of action and clinical results of Regelan (clofibrate)
AUTHOR(S): Fitzgerald, J. D.
CORPORATE SOURCE: Med. Dep., Macclesfield, UK
SOURCE: Wien. Klin. Wochenschr. (**1967**), 79(39), 716-20
DOCUMENT TYPE: Journal
LANGUAGE: German

AB Regelan (clofibrate) (25-30 mg./kg.) given daily to patients with increased serum lipid concns. reduced serum triglycerides 20-30%, serum cholesterol 15-30%, and phospholipids .apprx.30%. Regelan was only slightly absorbed but once in the bloodstream it rapidly and completely metabolized to chlorophenoxyisobutyric acid, 90% of which was bound to serum albumin. About 85% of the administered daily dose was excreted in the urine, mostly as a water-soluble glucuronide. Regelan did not affect globulin-bound thyroxine but cleaved prealbumin and albumin-bound thyroxine. Regelan was effective in the treatment of cardiac infarct, hyperlipidemia with xanthomatosis, and **diabetic retinopathy**. Regelan was free of toxic effects.

IT **882-09-7**
RL: BIOL (Biological study)
(as clofibrate metabolite)
RN 882-09-7 CAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl- (9CI) (CA INDEX NAME)



L18 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:58544 CAPLUS
DOCUMENT NUMBER: 88:58544
TITLE: Triglycerides, free fatty acids, and cholesterol after fat loading, clofibric acid treatment, and heparin injection in **diabetics** with and without hyperlipoproteinemia
AUTHOR(S): Singer, P.; Gnauck, G.; Honigmann, G.; Thoelke, H.; Schliack, V.; Laeuter, J.
CORPORATE SOURCE: Zentralinst. Herz- Kreislauf-Regulationsforsch., DAW, Berlin, Ger. Dem. Rep.
SOURCE: Deutsche Zeitschrift fuer Verdauungs- und Stoffwechselkrankheiten (**1977**), 37(1), 27-37
CODEN: DZVSAT; ISSN: 0012-1053
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Heparin [9005-49-6] (10,000 IU) injected i.v. into **diabetics** with and without hyperlipoproteinemia after fat loading (50 g butter) increased serum free fatty acids, decreased serum triglycerides, and had no effect on serum cholesterol [57-88-5]. In patients with hyperlipoproteinemia the decrease in serum triglycerides and the increase in serum fatty acids was dependent on the initial triglyceride levels. These results occurred whether or not the patient had been treated with Regadrin (clofibric acid) [**882-09-7**]. Patients with hyperlipoproteinemia but without carbohydrate metabolic disorders responded to heparin in the same manner as **diabetics** without hyperlipoproteinemia.
IT **882-09-7**
RL: BIOL (Biological study)
(heparin effect on serum lipids in **diabetics** with and without hyperlipoproteinemia in relation to)
RN 882-09-7 CAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl- (9CI) (CA INDEX NAME)

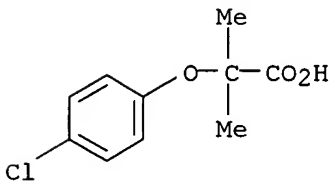


L18 ANSWER 3 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1974:22828 CAPLUS
DOCUMENT NUMBER: 80:22828
TITLE: Effect of propranolol and chlorophenoxyisobutyric acid on the dynamics of free fatty acids and blood sugar
AUTHOR(S): Haller, H.; Julius, U.; Leonhardt, W.; Hanefeld, M.
CORPORATE SOURCE: Med. Klin., Med. Akad. "Carl Gustav Carus", Dresden, Ger. Dem. Rep.
SOURCE: Deutsche Zeitschrift fuer Verdauungs- und Stoffwechselkrankheiten (**1972**), 32(5-6), 391-9
CODEN: DZVSAT; ISSN: 0012-1053
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The administration of 2-(4-chlorophenoxy)-2-methylpropanoic acid (Regadrin) [**882-09-7**] 4 times daily in 500 mg doses to insulin-taking **diabetics** having unbalanced metabolism produced a decrease in the blood free fatty acid level regardless of the metabolic state of the original material consumed. The **glucose** [50-99-7] assimilation coefficient was improved, but significant changes in the daily blood sugar profile did not occur and hypoglycemia was not observed Propranolol (I) [525-66-6] given 4 times daily in 25 mg doses decrased the blood free fatty acid level in the **diabetics** but did not affect carbohydrate degradation I can, nevertheless, be useful in subjects with advanced sympathicotonia and unbalanced metabolism The effect of Regadrin on blood free fatty acid level was reversible and did not continue after drug administration ceased. Precautions for use of I and Regadrin in cases of **diabetes** nellitus are discussed.

IT **882-09-7**
RL: BIOL (Biological study)
(blood sugar and fatty acid metabolism in **diabetes** in response to)

RN 882-09-7 CAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl- (9CI) (CA INDEX NAME)



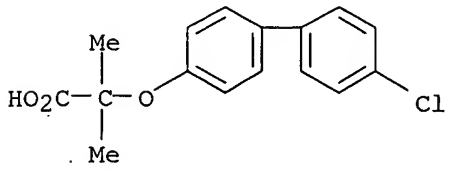
L23 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:57471 CAPLUS
DOCUMENT NUMBER: 70:57471
TITLE: Carboxylic acid derivatives with therapeutic properties
INVENTOR(S): Leigh, Thomas; Thorp, Jeffrey M.; Waring, Wilson S.
PATENT ASSIGNEE(S): Imperial Chemical Industries Ltd.
SOURCE: Brit., 18 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1121722		19680731	GB 1966-14264	19660331
DE 1593907			DE	
DE 1793705			DE	
FR 1524380			FR	
FR 6512			FR	
US 3652646		19720328	US	19670315
ZA 6701854		19670000	ZA	

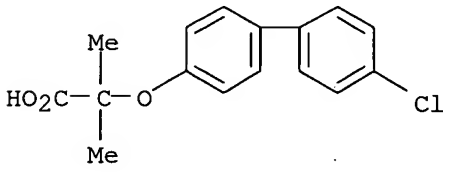
OTHER SOURCE(S): MARPAT 70:57471

AB Carboxylic acid derivs., and their esters and amides, are prepared and used to reduce the concentration of cholesterol and triglycerides in blood serum and fibrinogen in blood plasma, in the treatment of coronary artery disease and atherosclerosis. Thus, 2.5 parts NaH was added to a mixture of 20.4 parts 4-(p-chlorophenyl)phenol, and 300 parts HCONMe2, and stirred at room temperature 2 hrs. Et α-bromo-α-methylpropionate (25 parts) was added, the mixture stirred 12 hrs. and worked up to give 4-(4-R1C6H4)C6H4XCMe2COR2 (I, R1 = Cl, R2 = OH, X = O), m. 189-90°. Other I similarly prepared were, (R1, R2, X, and m.p. given): Cl, OEt, O, 44°; Cl, OMe, O, 90°; Cl, OH, O, 189-90°; Br, OH, O, 198-9°; Br, OMe, O, 101°; Br, OEt, O, 67°; NO2, OH, O, 185°; OMe, OH, O, 137-9°; OMe, OMe, O, 89°; Cl, OH, S, 129-30°; Cl, OMe, S, -, (b1 166°). To prepare I (X = S) the starting material, 4-(p-chlorophenyl)thiophenol, m. 150-1°, was prepared from 4-(p-chlorophenyl)benzenesulfonyl chloride, m. 104-6°, obtained from ClSO2OH and 4-ClC6H4Ph. Other similar derivs. prepared were, α-(2-chloro-6-phenylphenoxy)-α-methylpropionic acid, m. 134-5°, α-[2-chloro-4-(p-ethylphenyl)phenoxy]-α-methylpropionic acid, m. 145-6°, α-(2-chloro-4-phenylphenoxy)-α-methylpropionic acid, m. 109-11°, and methyl α-(2-chloro-4-phenylphenoxy)-α-methylpropionate, b. 162°. 4,3-ClPhC6H3OCMe2CONH2, m. 119-20°, was prepared from 3,4-R1ClC6H3OR2 (II, R1 = Ph, R2 = H), b. 127°, obtained from II (R1 = NO2, R2 = Me), m. 40-2°, via II (R1 = Ph, R2 = Me), b0.3 120°. Also prepared were p-ClC6H4C6H4OCHEtCO2H-p, m. 155°; p-ClC6H4C6H4OCMe-EtCO2H-p, m. 168°, and the following I (X, R1, R2, and m.p., given): SO, Cl, OH, 134°; SO2, Cl, OH, 199°; O, Cl, NH2, 171°; O, Cl, NMe2, 78°, O, Cl, NHMe, 149°; O, Cl, NHCH2CO2Me, 96°; O, Cl, OAl(OH)2·H2O, -; O, Cl, ONa.0.5 H2O, -; O, Cl, O.0.5 Ca, -; O, Cl, NHCH2CO2H, 160-1°; O, Cl, OCH2CH2, - (b0.1 180°); O, Et, OH, 131°; O, Cl, OCH2CH2NEt2·HCl, 158-9°; O, Cl, OCH2CH2NMe2·HCl, 150-2°; O, Cl, β-morpholinoethylamino, 132-4°; O, Cl, 1-pyrrolidinyl, 118-19°; O, CF3, OH, 184-5°. Also prepared was [4-(4-ClC6H4)-C6H4OCMe2CO2CH2]2CH2, m. 93°. The intermediate 4-(p-ethylphenyl)phenol, m. 151°, was also prepared The products were mixed with oil, or a gum, and formed into emulsions or tablets for oral administration.

IT **21340-66-9P 21345-23-3P 21345-24-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 21340-66-9 CAPLUS
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methyl- (9CI)
(CA INDEX NAME)

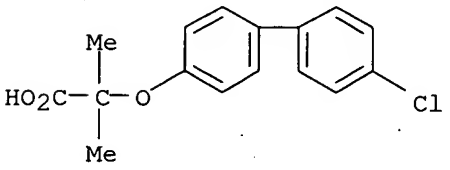


RN 21345-23-3 CAPLUS
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methyl-, sodium
salt (9CI) (CA INDEX NAME)



● Na

RN 21345-24-4 CAPLUS
CN Propionic acid, 2-[(4'-chloro-4-biphenylyl)oxy]-2-methyl-, calcium salt
(8CI) (CA INDEX NAME)



●1/2 Ca

IT 10298-80-3P 20443-74-7P **21340-66-9P** 21340-67-0P
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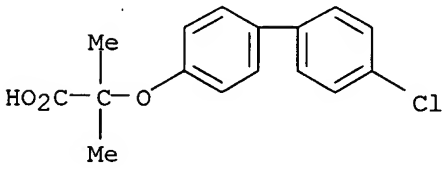
21340-73-8P 21340-74-9P 21340-75-0P 21340-76-1P 21340-77-2P
21340-78-3P 21340-79-4P 21340-80-7P 21345-09-5P 21345-10-8P
21345-12-0P 21345-13-1P 21345-14-2P 21345-15-3P 21345-16-4P
21345-17-5P 21345-18-6P 21345-19-7P 21345-20-0P 21345-21-1P
21345-22-2P **21345-23-3P 21345-24-4P** 21345-25-5P
21345-26-6P 21345-27-7P 21345-28-8P 21345-29-9P 21345-30-2P
21345-31-3P 21345-33-5P 21345-34-6P 21401-41-2P 23383-05-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L23 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1970:74999 CAPLUS
DOCUMENT NUMBER: 72:74999
TITLE: Mode of action of lipid-lowering agents. II. In vitro inhibition of acetyl coenzyme A carboxylase by a hypolipidemic drug
AUTHOR(S): Maragoudakis, Michael E.
CORPORATE SOURCE: Res. Dep., CIBA Pharm. Co., Summit, NJ, USA
SOURCE: Biochemistry (1970), 9(2), 413-17
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Acetyl coenzyme A carboxylase, a key enzyme in lipid biosynthesis, is being assessed as a possible locus of action for hypolipidemic agents. 2-Methyl-2-[p-(p-chlorophenyl)phenoxy]propionate, a newly described lipid-lowering agent, strongly inhibits hepatic acetyl coenzyme Acarboxylase from chickens or rats. Kinetic anal. of the inhibition suggests that the inhibition is competitive for acetyl coenzyme A and isocitrate and noncompetitive for ATP and HCO3-. The values of the kinetic consts. obtained are Km = 8 + 10-5M for acetyl coenzyme A and Ki = 1.5 + 10-4M for acetyl coenzyme A as varying substrate; Km = 1.25 + 10-3M for isocitrate and Ki = 7.9 + 10-5M for varying isocitrate concns.; Km = 2.1 + 10-3M for ATP and Ki = 2.8 + 10-4M for ATP as varying substrate; and Km = 1.5 + 10-2M for HCO3- and Ki = 3.4 +10-4M for varying HCO3- concns.

IT **26437-29-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypolipidemic activity of, acetyl coenzyme A carboxylase in relation to)

RN 26437-29-6 CAPLUS
CN Propionic acid, 2-[p-(p-chlorophenyl)phenoxy]-2-methyl-, potassium salt (8CI) (CA INDEX NAME)



● K

IT Lipids
RL: BIOL (Biological study)
(blood, lowering of, acetyl coenzyme A carboxylase inhibition in relation to)

IT Kinetics, enzymic
(of inhibition, of acetyl coenzyme A carboxylase)

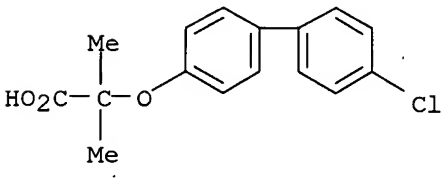
IT **26437-29-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypolipidemic activity of, acetyl coenzyme A carboxylase in relation to)

IT 9023-93-2, Carboxylases, acetyl coenzyme A
(inhibition of, by hypolipidemic compds.)

L23 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:84007 CAPLUS
DOCUMENT NUMBER: 84:84007
TITLE: Drugs affecting the synthesis of glycerides and phospholipids in rat liver. Effects of clofibrate, halofenate, fenfluramine, amphetamine, cinchocaine, chlorpromazine, demethylimipramine, mepyramine, and their derivatives
AUTHOR(S): Brindley, David N.; Bowley, Mariana
CORPORATE SOURCE: Dep. Biochem., Univ. Hosp., Nottingham, UK
SOURCE: Biochemical Journal (1975), 148(3), 461-9
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In cell-free prepns. and slices of rat liver, clofenapate [**21345-23-3**] and 2-(p-chlorophenyl)-2-(m-trifluoromethylphenoxy)acetate [4687-08-5] inhibited glycerol phosphate acyltransferase (I) [9029-96-3] and diacylglycerol acyltransferase (EC 2.3.1.20) (II) [9029-98-5] activities at .apprx.1.6 and 0.7mM, resp. Mepyramine maleate [59-33-6], fenfluramine [458-24-2], norfenfluramine HCl, hydroxyethylnorfenfluramine [31173-14-5], S780 [23602-78-0], cinchocaine [85-79-0], chlorpromazine [50-53-3], and demethylimipramine [50-47-5] inhibited phosphatidate phosphohydrolase (EC 3.1.3.4) [9025-77-8] 50% at 0.2-0.9mM. The last 4 compds. also inhibited I by 50% at 1-2.6mM. Norfenfluramine and its derivs. inhibited glycerol incorporation into total lipids less than clofenapate which, at 1mM, inhibited incorporation without affecting the relative proportions of different lipids formed. P-chlorobenzoate [74-11-3], p-chlorophenoxyisobutyrate [882-09-7], halofenate [26718-25-2], D-amphetaminesulfate [51-63-8], adrenaline [51-43-4], procaine [51-05-8], and S1204 [23189-05-1] had little inhibitory effect on glycerolipid formation in any of the systems studied. The results, which are discussed in terms of the control of glycerolipid formation, partly explain the observed effects of the pharmaceuticals on lipid metabolism The possible use of these compds. as biochem. tools with which to investigate the reactions of glycerolipid formation is considered.

IT **21345-23-3**
RL: BIOL (Biological study)
(glyceride and phospholipid formation by liver response to)
RN 21345-23-3 CAPLUS
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methyl-, sodium salt (9CI) (CA INDEX NAME)



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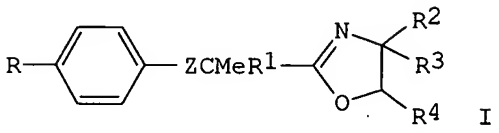
IT Glycerides, biological studies
Phospholipids
RL: FORM (Formation, nonpreparative)
(formation of, by liver, pharmaceuticals effect on)
IT Liver, metabolism

(of glycerides and phospholipids, pharmaceuticals effect on)
IT 50-47-5 50-53-3, biological studies 51-05-8 51-43-4 51-63-8
59-33-6 61-12-1 74-11-3 458-24-2 673-18-7 882-09-7 4687-08-5
21345-23-3 23189-05-1 23602-78-0 26718-25-2 31173-14-5
RL: BIOL (Biological study)
(glyceride and phospholipid formation by liver response to)
IT 9025-77-8 9029-96-3 9029-98-5
RL: BIOL (Biological study)
(of liver, pharmaceuticals effect on, glyceride and phospholipid formation in relation to)

L23 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:421604 CAPLUS
DOCUMENT NUMBER: 85:21604
TITLE: 2-oxazoline derivatives
INVENTOR(S): Toth, Istvan T.; Bite, Pal; Magyar, Gyorgy; Diszler, Eszter; Borsy, Jozsef; Maderspach, Andrea; Polgari, Istvan; Elek, Sandor; Elekes, Istvan
PATENT ASSIGNEE(S): Chinoin Gyogyszer Es Vegyeszeti Termekek Gyara Rt., Hung.
SOURCE: Brit., 9 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1426028	A	19760225	GB 1973-48936	19731019
HU 167760	P	19751225	HU 1972-GO1222	19721020
DK 135991	B	19770725	DK 1973-5618	19731017
DD 108753	Z	19741012	DD 1973-174182	19731018
AT 7308835	A	19751215	AT 1973-8835	19731018
AT 331791	B	19760825		
SE 386173	B	19760802	SE 1973-14214	19731018
FI 57405	B	19800430	FI 1973-3243	19731018
FI 57405	C	19800811		
NL 7314414	A	19740423	NL 1973-14414	19731019
ES 419969	A1	19760801	ES 1973-419969	19731019
SU 539528	D	19761215	SU 1973-1966754	19731019
CA 1021343	A1	19771122	CA 1973-183698	19731019
CH 602677	A	19780731	CH 1973-14810	19731019
NO 141648	B	19800107	NO 1973-4058	19731019
NO 141648	C	19800416		
PL 89478	P	19760630	PL 1973-165975	19731020
BE 806342	A1	19740215	BE 1973-136916	19731022
CS 181838	B	19780331	CS 1973-7264	19731022

PRIORITY APPLN. INFO.: HU 1972-GO1222 A 19721020
GI

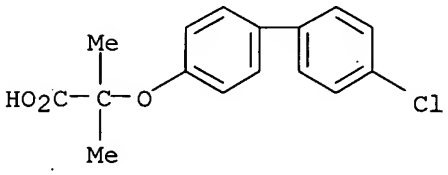


I

AB Nineteen title compds. I (R = Cl, Br, Ph, 4-ClC6H4; R1 = H, Me, Et; R2, R3 = H, alkyl, HOCH2; R4 = H, Me, Et2NCH2, CH2:CHCH2OCH2; Z = O, S, NH), useful as hypolipemic and hypocholesteremic agents, were prepared (30-88%) from 4-RC6H4ZCMeR1R5 (R5 = CN, CO2H) by treatment with H2NCR2R3CHR4OH in the presence of Na alkoxide or a soluble Zn or Cd salt. Thus, I (R = Cl, R1 = R2 = R3 = Me, R4 = H, Z = O) was prepared (88%) from 4-ClC6H4OCMe2CN by treatment with H2NCMe2CH2OH in a 1:2 molar ratio in the presence of (AcO)2Zn for 34 hr at 140-50°. The hypocholesteremic and hypolipemic activities of I were assessed in rats; at doses of 30-150 mg/kg I showed effects comparable to those of Atromid S at doses of 300 mg/kg. I showed no toxicity at oral doses of 1000 mg/kg.

IT **21340-66-9**
RL: RCT (Reactant); RACT (Reactant or reagent)

(cyclocondensation with amino alcs., oxazoline derivs. by)
RN 21340-66-9 CAPLUS
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methyl- (9CI) (CA INDEX NAME)



IT Blood
(cholesterol of, oxazoline derivs. for lowering of)
IT Nitriles, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation with amino alcs., oxazolines by)
IT Lipids
RL: RCT (Reactant); RACT (Reactant or reagent)
(of blood, oxazoline derivs. for lowering of)
IT 882-09-7 18518-83-7 **21340-66-9** 24889-11-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation with amino alcs., oxazoline derivs. by)
IT 77-86-1 115-69-5 115-70-8 124-68-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation with aryloxyalkyl nitriles, oxazoline derivs. by)
IT 21345-17-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(dehydration of)
IT 52800-80-3P 52800-81-4P 52800-82-5P 52800-83-6P 52800-84-7P
52800-85-8P 52800-86-9P 52800-87-0P 52800-88-1P 52800-89-2P
52800-90-5P 52800-91-6P 52800-92-7P 52800-93-8P 52800-97-2P
52844-92-5P 52844-93-6P 52844-94-7P 54030-06-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(hypocholesteremic and hypolipemic agent, preparation of)
IT 57-88-5, biological studies
RL: BIOL (Biological study)
(of blood, oxazoline derivs. for lowering of)
IT 52800-95-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation with amino alcs.)

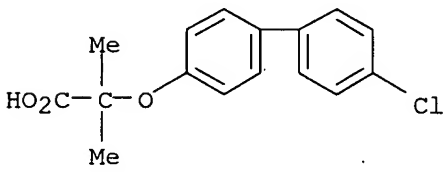
L23 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:84007 CAPLUS
DOCUMENT NUMBER: 84:84007
TITLE: Drugs affecting the synthesis of glycerides and phospholipids in rat liver. Effects of clofibrate, halofenate, fenfluramine, amphetamine, cinchocaine, chlorpromazine, demethylimipramine, mepyramine, and their derivatives
AUTHOR(S): Brindley, David N.; Bowley, Mariana
CORPORATE SOURCE: Dep. Biochem., Univ. Hosp., Nottingham, UK
SOURCE: Biochemical Journal (1975), 148(3), 461-9
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In cell-free prepns. and slices of rat liver, clofenapate [**21345-23-3**] and 2-(p-chlorophenyl)-2-(m-trifluoromethylphenoxy)acetate [4687-08-5] inhibited glycerol phosphate acyltransferase (I) [9029-96-3] and diacylglycerol acyltransferase (EC

2.3.1.20) (II) [9029-98-5] activities at .apprx.1.6 and 0.7mM, resp. Mepyramine maleate [59-33-6], fenfluramine [458-24-2], norfenfluramine HCl, hydroxyethylnorfenfluramine [31173-14-5], S780 [23602-78-0], cinchocaine [85-79-0], chlorpromazine [50-53-3], and demethylimipramine [50-47-5] inhibited phosphatidate phosphohydrolase (EC 3.1.3.4) [9025-77-8] 50% at 0.2-0.9mM. The last 4 compds. also inhibited I by 50% at 1-2.6mM. Norfenfluramine and its derivs. inhibited glycerol incorporation into total lipids less than clofenapate which, at 1mM, inhibited incorporation without affecting the relative proportions of different lipids formed. P-chlorobenzoate [74-11-3], p-chlorophenoxyisobutyrate [882-09-7], halofenate [26718-25-2], D-amphetaminesulfate [51-63-8], adrenaline [51-43-4], procaine [51-05-8], and S1204 [23189-05-1] had little inhibitory effect on glycerolipid formation in any of the systems studied. The results, which are discussed in terms of the control of glycerolipid formation, partly explain the observed effects of the pharmaceuticals on lipid metabolism The possible use of these compds. as biochem. tools with which to investigate the reactions of glycerolipid formation is considered.

IT **21345-23-3**
RL: BIOL (Biological study)
(glyceride and phospholipid formation by liver response to)

RN 21345-23-3 CAPLUS

CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methyl-, sodium salt (9CI) (CA INDEX NAME)



IT Glycerides, biological studies
Phospholipids
RL: FORM (Formation, nonpreparative)
(formation of, by liver, pharmaceuticals effect on)

IT Liver, metabolism
(of glycerides and phospholipids, pharmaceuticals effect on)

IT 50-47-5 50-53-3, biological studies 51-05-8 51-43-4 51-63-8 59-33-6 61-12-1 74-11-3 458-24-2 673-18-7 882-09-7 4687-08-5 **21345-23-3** 23189-05-1 23602-78-0 26718-25-2 31173-14-5
RL: BIOL (Biological study)
(glyceride and phospholipid formation by liver response to)

IT 9025-77-8 9029-96-3 9029-98-5
RL: BIOL (Biological study)
(of liver, pharmaceuticals effect on, glyceride and phospholipid formation in relation to)

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L3                STRUCTURE UPLOADED
L4              6 S SSS L2 FULL
L5                STRUCTURE UPLOADED
L6            190 S SSS FULL L5
L7            196 S L2 OR L4 OR L6

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L9            331 S L8 AND (HEART OR CARDIO? OR STROKE OR COMA OR KIDNEY DISEASE
L10           283 DUP REM L9 (48 DUPLICATES REMOVED)
L11           283 FOCUS L10 1-
L12            78 S L10 AND (DIABETIC OR DIABETE OR GLUCOSE)
L13            78 FOCUS L12 1-
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L17           213 S L9 AND PD <=1999
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L21             0 S L9 NOT L7
L22          3062 S L2 OR L6
L23            11 S L2 OR L4

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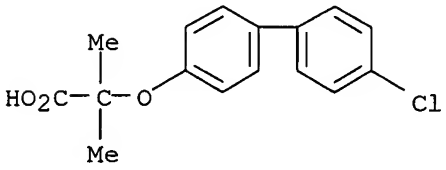
ANSWER 1 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 71711-76-7 REGISTRY
ED Entered STN: 16 Nov 1984
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methyl-, compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethanamine, N,N-diethyl-, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methylpropanoate
MF C16 H15 Cl O3 . C6 H15 N
LC STN Files: CA, CAPLUS

CM 1

CRN 21340-66-9
CMF C16 H15 Cl O3



CM 2

CRN 121-44-8
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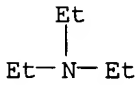
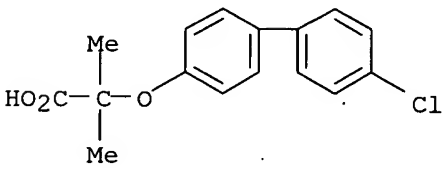


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 26437-29-6 REGISTRY
ED Entered STN: 16 Nov 1984
CN Propionic acid, 2-[p-(p-chlorophenyl)phenoxy]-2-methyl-, potassium salt (8CI) (CA INDEX NAME)
OTHER NAMES:
CN Potassium 2-methyl-2-[p-(p-chlorophenyl)phenoxy]propionate
MF C16 H15 Cl O3 . K
LC STN Files: CA, CAPLUS
CRN (21340-66-9)



L18 ANSWER 16 OF 53 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

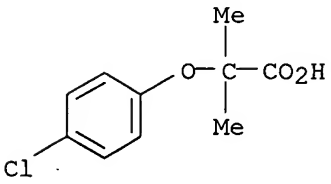
ACCESSION NUMBER: 78162935 EMBASE
DOCUMENT NUMBER: 1978162935
TITLE: Effect of clofibrate on **glucose** tolerance in maturity onset **diabetes**.
AUTHOR: Barnett D.; Craig J.G.; Robinson D.S.; Rogers M.P.
CORPORATE SOURCE: St James's Univ. Hosp., Leeds, United Kingdom
SOURCE: British Journal of Clinical Pharmacology, (**1977**) Vol. 4, No. 4, pp. 455-458. .
CODEN: BCPHBM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
003 Endocrinology
006 Internal Medicine
LANGUAGE: English

AB 1. Fourteen maturity onset **diabetics** showed improvement of **glucose** tolerance while on treatment with clofibrate. Fasting blood **glucose** levels were reduced by 20% after treatment for 14 and 28 days. 2. The effect was found to be independent of current treatment with oral hypoglycaemic drugs. 3. Plasma insulin levels also lower during clofibrate treatment. 4. Clofibrate may prove to be a useful adjunct to the treatment of maturity onset **diabetes**.

L18 ANSWER 27 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:526893 CAPLUS
DOCUMENT NUMBER: 107:126893
TITLE: Effect of long-term clofibric acid treatment on serum and tissue lipid and cholesterol levels in obese Zucker rats
AUTHOR(S): Cleary, Margot P.; Kasiske, Bertram; O'Donnell, Michael P.; Keane, William F.
CORPORATE SOURCE: Hormel Inst., Univ. Minnesota, Austin, MN, 55912, USA
SOURCE: Atherosclerosis (Shannon, Ireland) (**1987**), 66(1-2), 107-12
CODEN: ATHSBL; ISSN: 0021-9150
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The long-term effects of clofibric acid (200 mg/kg) injected s.c. from 6-36 wk of age were assessed in obese, hyperlipemic Zucker rats. At 18 and 36 wk of age, treated rats had lower fasted serum cholesterol levels but triacylglycerol levels were not affected. Rats were killed at 36 wk of age at which time there were no differences in body and kidney wts. between control and clofibric acid-treated rats. Liver, spleen and **heart** wts. were lowered by clofibric acid treatment. In liver there was an elevation of lipid/g due to treatment but there were no effects on cholesterol/g or on either total liver lipid or cholesterol levels. In the epididymal fat pad of clofibric acid-treated rats, there was a 21% elevation of cholesterol level on a per pad basis. In the other organs, there were no effects of treatment on lipid or cholesterol levels except for lowered total cholesterol in kidney. Several liver lipogenic enzymes were lowered by treatment but malic enzyme was 2 times higher.

IT **882-09-7**, Clofibric acid
RL: BIOL (Biological study)
(cholesterol and lipid metabolism response to)
RN 882-09-7 CAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl- (9CI) (CA INDEX NAME)

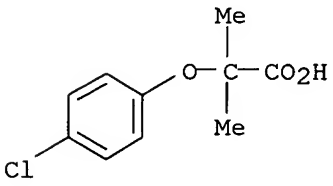


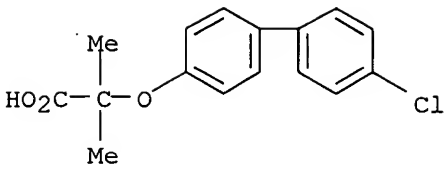
L18 ANSWER 30 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:587269 CAPLUS
DOCUMENT NUMBER: 111:187269
TITLE: Co-induction by peroxisome proliferators of microsomal 1-acylglycerophosphocholine acyltransferase with peroxisomal β-oxidation in rat liver
AUTHOR(S): Kawashima, Yoichi; Horii, Sachiko; Matsunaga, Tomomi; Hirose, Akihiko; Adachi, Toshiyuki; Kozuka, Hiroshi
CORPORATE SOURCE: Fac. Pharm. Sci., Toyama Med. Pharm. Univ., Toyama, Japan
SOURCE: Biochimica et Biophysica Acta, Lipids and Lipid Metabolism (**1989**), 1005(2), 123-9
CODEN: BBLLA6; ISSN: 0005-2760
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Administration of clofibric acid, 2,2'-(decamethylenedithio)diethanol, di-(2-ethylhexyl)phthalate, or perfluorooctanoic acid to male rats increased markedly liver microsomal 1-acylglycerophosphocholine (1-acyl-GPC) acyltransferase in a dose-dependent manner. Simultaneous administration of actinomycin D or cycloheximide completely abolished the increase in the enzyme activity. The treatment of rats with clofibric acid did not affect the rate of decay of 1-acyl-GPC acyltransferase. Despite a great difference in the chemical structures of the peroxisome proliferators, a high correlation was observed between the induced activities of microsomal 1-acyl-GPC acyltransferase an peroxisomal β-oxidation Stearoyl-CoA desaturase was induced by peroxisome proliferators in a dose-dependent manner; nevertheless, a high correlation was not seen between the induced activities of desaturase and peroxisomal β-oxidation Hormonal (adrenalectomy, **diabetes**, hyperthyroidism, and hypothyroidism) and nutritional (starvation, starvation-refeeding, fat-free diet feeding, and high-fat diet feeding) alterations hardly affected the activity of 1-acyl-GPC acyltransferase. Thus, microsomal 1-acyl-GPC acyltransferase is a useful parameter responsive to the challenges by peroxisome proliferators and a similar regulatory mechanism operates for the inductions of microsomal 1-acyl-GPC acyltransferase and peroxisomal β-oxidation

IT **882-09-7**
RL: BIOL (Biological study)
(acylglycerophosphocholine acyltransferase and β-oxidation in liver increase by)

RN 882-09-7 CAPLUS
CN Propanoic acid, 2-(4-chlorophenoxy)-2-methyl- (9CI) (CA INDEX NAME)





● Na

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 21340-66-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)oxy]-2-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propionic acid, 2-[(4'-chloro-4-biphenylyl)oxy]-2-methyl- (8CI)
OTHER NAMES:
CN Clofenapic acid
CN ICI 54856
MF C16 H15 Cl O3
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
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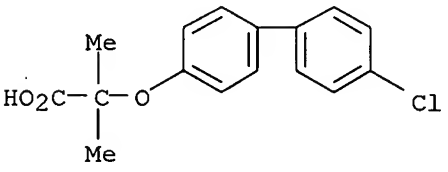

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DIABETES

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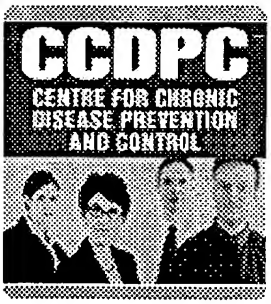


What are the complications of Diabetes?

Diabetes potentially affects the metabolism of every cell in the body and adversely affects the body's blood supply. Over a period of months or years, it can lead to a wide range of life-threatening and disabling complications. But these can often be prevented or substantially delayed with the help of intensive diabetes therapy consistently applied, by individuals with diabetes along with their care team.

Diabetic ketoacidosis (diabetic coma)
Uncontrolled diabetes in a person with type 1 diabetes can lead to potentially fatal dehydration and metabolic imbalance known as diabetic ketoacidosis (diabetic coma). This is an emergency situation, which can almost always be prevented through good control of the diabetes. Sometimes, the occurrence of ketoacidosis is the clinician's first indicator that type 1 diabetes is present.

Fast Facts

Life Threatening Complications:

Diabetic ketoacidosis (diabetic coma)

Nonketotic hyperglycaemic-hyperosmolar coma (NKHHC)

Hypoglycemia

Nonketotic hyperglycaemic-hyperosmolar coma (NKHHC)
A similar condition, known as nonketotic hyperglycaemic-hyperosmolar coma (NKHHC), can occur in type 2 diabetes. It, too, is associated with dehydration and preceded by a period of poor control of diabetes. NKHHC has a 50% mortality rate.

Improvements in diabetes management appear to have reduced the incidence of these two complications in Canada and other industrialized countries. When they do occur, it is usually as a result of infection, poor compliance or dehydration.

Hypoglycemia (low blood sugar) can result from an excess of either insulin or oral diabetes medication. Usually, hypoglycemia is managed by consuming a sugar product or fruit juice. Most hypoglycemic reactions are mild, and people with diabetes and their families are trained to recognize them and self-administer the sugar needed to correct the situation. In the case of severe low blood sugar resulting in coma the use of glucagon and/or the assistance of a health professional may be required.

Long-term complications

Cardiovascular (heart) disease and stroke
Diabetes increases the risk of cardiovascular problems, including heart attacks and strokes.

Fast Facts

Diabetes is a major

Canadian data indicate that people aged 35 to 64 who have diabetes are six times more likely to have heart disease or stroke than non-diabetics in the same age group.

High blood pressure
It is estimated that 60 to 65 percent of people with diabetes also have high blood pressure, increasing their risk of stroke, heart disease and kidney disease. The good news: controlling their blood pressure and blood glucose levels can help people at risk avoid many of these problems.

Lower-limb amputations
Having diabetes increases the risk of lower-limb amputation some fifteen-fold. At highest risk are those over age 40 whose diabetes diagnosis dates back at least 10 years.
The good news: Good foot care and aggressive treatment can substantially reduce the risk for lower-limb amputation.

cause of other diseases or chronic conditions. But these can often be prevented or substantially delayed with intensive diabetes therapy.

- heart-disease and stroke
- high blood pressure
- lower-limb amputations
- eye disease (retinopathy)
- kidney disease
- nervous system disorders
- pregnancy complications
- other (influenza, pneumonia, etc.)

Diabetic eye disease (retinopathy)
Diabetic retinopathy (DR) is the leading cause of vision loss in working-age adults in both Canada and North America as a whole. The Canadian National Institute for the Blind (CNIB), which is the largest vision rehabilitation agency in Canada, reports that over the past three years DR has been the second leading cause of vision loss for its clients in all age groups.

The good news: People with diabetes can prevent or delay vision loss or blindness due to DR through proper control of blood sugar. DR develops slowly over time, and may be quite advanced before symptoms of vision loss appear. Fortunately, treatment with laser light during the developmental period can slow the progress of the condition. Eye examinations at appropriate intervals, by suitably trained health professionals, allow a determination to be made as to whether such treatment is needed.

Kidney disease
The number of Canadians with newly diagnosed kidney failure who also have diabetes nearly doubled in the 15 years between 1981 and 1996 (from 16% to 28%). By the end of 1996, over 3,300 Canadians with diabetes were being treated for kidney failure, usually by dialysis.

The good news: Diabetes-related kidney disease can often be prevented or its progress markedly slowed. Proper control of blood sugars is required, as well as regular monitoring of protein loss in the urine, enabling kidney problems to be diagnosed earlier and treated more aggressively.

Nervous system disorders
About one-half of those with diabetes experience problems with the transmission of nerve impulses. Ranging from mild to severe, these can produce disabling conditions such as impaired sensation and/or pain in the feet and hands, carpal tunnel syndrome, slowed digestion of food, impotence, as well as other problems of the nervous system.

When impaired sensation in the feet occurs, minor injuries in that area may become infected and progress without being noticed. This sometimes culminates in amputation of the feet and/or legs.

The good news: Close control of blood sugar and regular examination of the feet may prevent this type of complication.

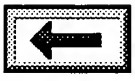
Other complications

People with diabetes have a higher susceptibility to infectious illnesses, such as boils and yeast infections. They are also more likely to die of pneumonia or influenza than people who do not have diabetes.

The good news: Immunizations against influenza and pneumonia can protect individuals with diabetes from these particular infections.

Last Updated: 2003-01-17 ▲ Important Notices

Diabetes Mellitus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The images below have file sizes ranging from 50 to 250k.

Pancreas

The islets of Langerhans are destroyed in type I diabetes mellitus. This occurs probably as a consequence of a genetic susceptibility, followed by the onset of autoimmune destruction triggered by some environmental factor such as a viral infection. Heavy lymphocytic infiltrates appear in and around islets. The number and size of islets are eventually reduced, leading to decreased insulin production and glucose intolerance.

The islets of Langerhans are normal in number or somewhat reduced with type II diabetes mellitus. Fibrosis and deposition of amylin polypeptide within islets are most characteristic of the chronic states of type II diabetes.

1. **Normal islets of Langerhans, with immunoperoxidase stains (right, insulin and left, glucagon), microscopic.**
2. **Islet of Langerhans, insulitis, microscopic.**
3. **Islet of Langerhans, deposition of amyloid, microscopic.**

Renal Complications

There are a variety of complications involving the kidney. Both nodular and diffuse glomerulosclerosis can lead to chronic renal failure. Diabetics are prone to infections, particularly pyelonephritis. Both bacterial and fungal infections can occur.

1. **Renal glomerulus, nodular glomerulosclerosis, microscopic.**
2. **Renal glomerulus, nodular glomerulosclerosis, hyaline arteriolosclerosis, PAS stain, microscopic.**
3. **Kidney, acute pyelonephritis, microscopic.**
4. **Renal pelvis, infection with Candida albicans, PAS stain, microscopic.**

Ocular Complications

The eyes can be affected in several ways by diabetes mellitus. Diabetic retinopathy is one of the leading causes for irreversible blindness in the United States. This retinopathy can occur with either type I or type II diabetes mellitus, usually a decade or so after the onset of diabetes. Most persons with type I diabetes and many of those with type II diabetes develop some background (non-proliferative) retinopathy. Proliferative retinopathy is more ominous and is more likely to occur when diabetes mellitus is poorly controlled.

In severe retinopathy, neovascularization may lead to adhesions (synechiae) between iris and cornea or iris and lens. Neovascularization of the iris leads to secondary glaucoma with blindness.

Cataracts are more common in diabetics. This predilection for development of cataracts is felt to result from hyperglycemia leading to accumulation of sorbitol that results in osmotic damage to the crystalline lens.

1. **Normal appearance, retina on funduscopic examination.**
2. **Diabetic retinopathy on funduscopic examination.**
3. **Proliferative diabetic retinopathy on funduscopic examination.**
4. **Glaucoma, cupping of the optic disk on funduscopic examination.**
5. **Glaucoma with excavation of the optic cup, microscopic.**
6. **Cataract of the crystalline lens, gross.**

Atherosclerosis

Persons with diabetes mellitus, either type I or type II, have early and accelerated **atherosclerosis**. The most serious complications of this are atherosclerotic heart disease, cerebrovascular disease, and renal disease. The most common cause of death with diabetes mellitus is myocardial infarction.

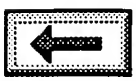
Peripheral vascular disease is a particular problem with diabetes mellitus and is made worse through the development of diabetic neuropathy, leading to propensity for injury.

1. **Left anterior descending coronary artery, advanced atherosclerosis, gross.**
2. **Left anterior descending coronary artery, recent thrombus, microscopic.**
3. **Interventricular septum, recent myocardial infarction, gross.**
4. **Aortic atherosclerosis demonstrated in three aortas, gross.**
5. **Foot with previous healed transmetatarsal amputation and recent ulcer, gross.**
6. **Gangrenous necrosis and ulceration, lower extremity, gross.**

Mucormycosis

This is a feared **complication** of diabetes mellitus. Diabetic ketoacidosis helps to potentiate the growth of Mucor. The site of involvement is typically the nasopharyngeal region, but the infection can spread to involve soft tissues and bone of the face, orbit, skull, and brain.

1. **Nasopharynx, mucormycosis (zygomycosis), H and E stain, microscopic.**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Diabetes Complications

Chronic Complications of Diabetes: Long-Term Problems

Until recently, Acute complications were the primary causes of death in people with diabetes. With the discovery of insulin, diabetic ketoacidosis and hyperosmolar coma are relatively easily to prevent and treatment is common.

Long term complications are a different story. You can however, dramatically reduce your risk of all the major complications of diabetes by working with your Diabetes health care team to keep your blood sugar levels in tight control and keep them as closely to normal as possible.

The main challenge is that keeping your blood glucose levels normal is necessary for optimum prevention of long-term complications, and such precise control is easier said then done. In some cases, strict care to keep blood sugar levels low may not even be safe or appropriate. Some researchers think long term complications don't start till puberty and keeping children under a certain age can be dangerous and unnecessary.

Eye Problems

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There are three types of complications that can affect someone with diabetes. **Diabetic retinopathy**--damage to the blood vessels

in the retina. This is the leading cause of blindness. **Cataract**--clouding of the eye's lens. **Glaucoma**--increase in fluid pressure inside the eye that leads to optic nerve damage and loss of vision. For more on eye complications click here.

Kidney Problems

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High blood sugar can also affect the kidneys. Damage to the kidneys related to diabetes is called *diabetic nephropathy*. Diabetes may damage the tiny filtration units in the kidneys, or result in **atherosclerosis** blocking the important arteries feeding the kidneys. Extensive kidney damage can result in renal failure—the kidneys no longer work—and the patient must have a kidney transplant or be placed on dialysis.

The best ways to prevent this condition are controlling the blood sugar and taking steps to prevent **atherosclerosis**. For more on kidney complications click here.

Nerve Damage

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Just as it can affect blood vessels, Chronically high blood sugar can damage nerves. People with long-term diabetes may experience pain or numbness in the arms, legs, and especially the feet. This is called *diabetic peripheral neuropathy*. Neuropathy, or nerve damage, can also affect the nerves controlling internal organs and structures. This so-called *autonomic neuropathy* can cause a variety of symptoms and conditions.

For example, if diabetes damages the nerves that control the intestines, the person may alternate between constipation and diarrhea. Neuropathy can also affect the heart, causing abnormal rhythms. Some people with long-term diabetes experience balance problems, dizziness, and impotence.

As for all other diabetic complications, the best approach to preventing nerve damage is to keep blood sugar levels under good control. For more information on nerve complications click here.

Circulation Problems, Heart Disease, and Stroke

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Chronically high blood sugar can damage large and small blood vessels, accelerating the development of **atherosclerosis** (hardening of the arteries) as well as causing other forms of damage unique to diabetes. **Atherosclerosis** in turn causes heart attacks, strokes, kidney damage, and loss of circulation in the legs. People who have had diabetes for at least 10 years have twice the prevalence of coronary artery diseases as nondiabetics.

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What's New!!

Get the Pink Panther book

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A diabetic can take many steps to reduce the risk of developing **atherosclerosis**, including keeping good control of blood sugar levels, reducing cholesterol, and lowering blood pressure. For more information on heart disease click here.

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- contact office
- seminars
- contact Board of Directors
- dictionary Online
- Diabetes Type II Risk Calculator

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- **DSSC Seminars**

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